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(56) Documents cited

GB 2151491 A	GB 2142246 A	GB 2129691 A
GB 2103564 A	GB 2064336 A	GB 1515265 A
GB 1472650 A	GB 1331216 A	GB 0818365 A
GB 0676568 A	GB 0588117 A	GB 0576047 A
GB 0563011 A	GB 0456471 A	GB 0428635 A
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US 4095596 A		

(58) Field of search
UK CL (Edition K) A5T TBD TBE, B8C
INT CL⁵ A61J, A61M
Online databases: WPI, CLAIMS

(54) Inhalation apparatus and fracturable capsule for use therewith

(57) A capsule (2) containing an inhalant medicament is so formed as to be readily fracturable to release the medicament into the air stream of an inhaler device. Preferably the capsule has areas of reduced cross section, but may be merely formed from readily crushable or fracturable material.

The inhaler comprises a body having a mesh grid (48) on which the capsule sits, and part of the body (34) is movable with respect to the capsule in order to apply pressure to it and fracture it, using grid (50).

A further grid (52) between the capsule and a mouth piece ensures that only the medicament exits through the mouth piece into the patient's airways.

FIG.12

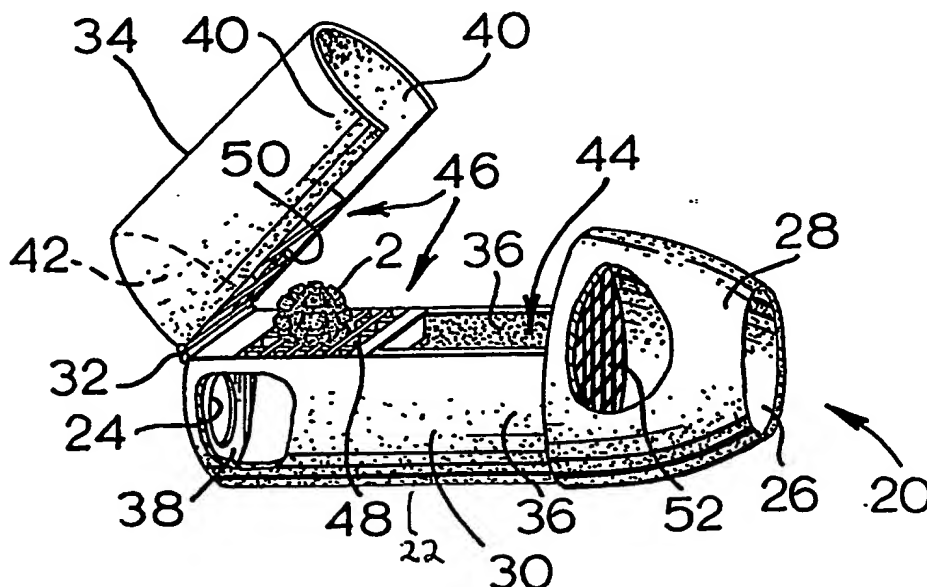


FIG. 1

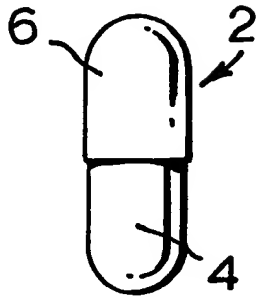


FIG. 2

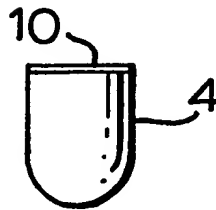


FIG. 3

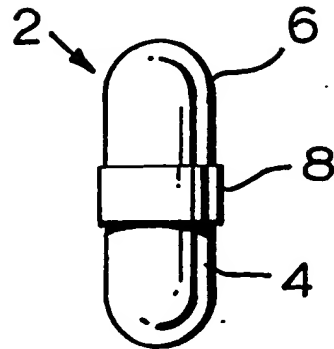


FIG. 4

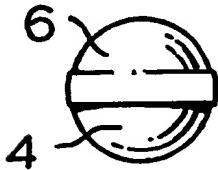


FIG. 5

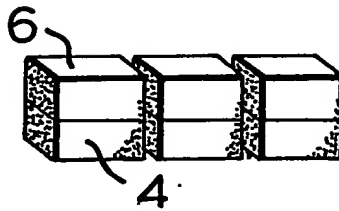


FIG. 6

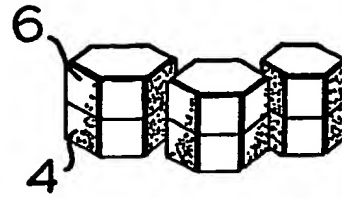


FIG. 7

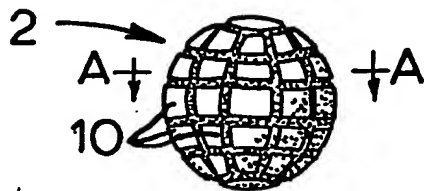


FIG. 8

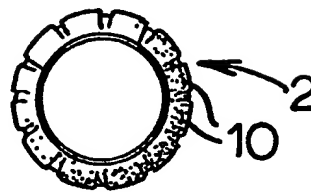


FIG. 9

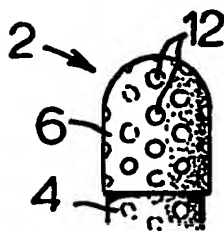


FIG. 10

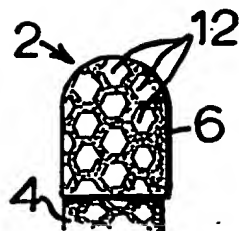


FIG. 11

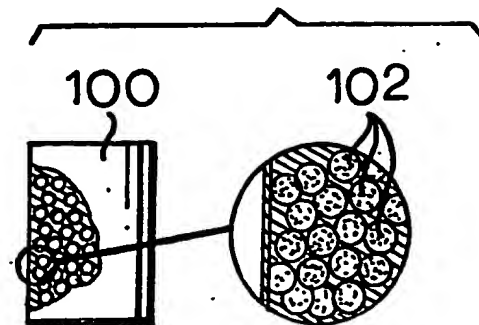


FIG.12

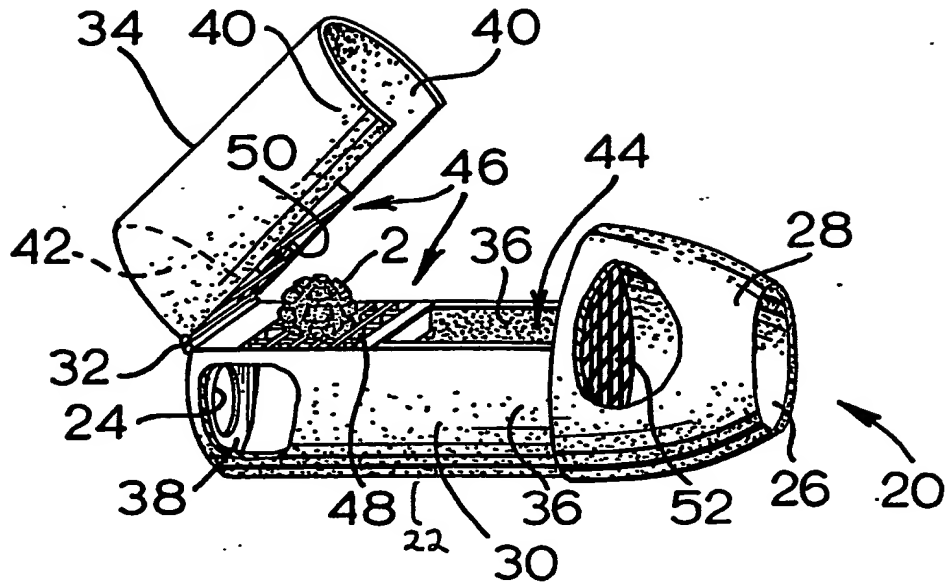


FIG.13

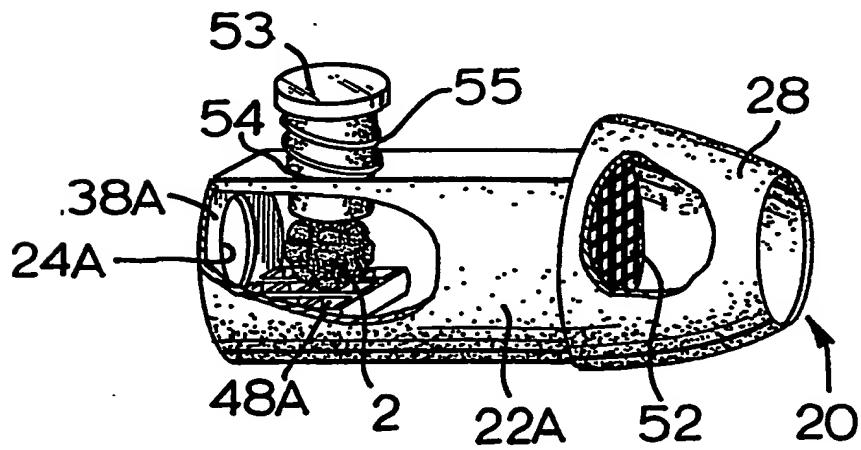
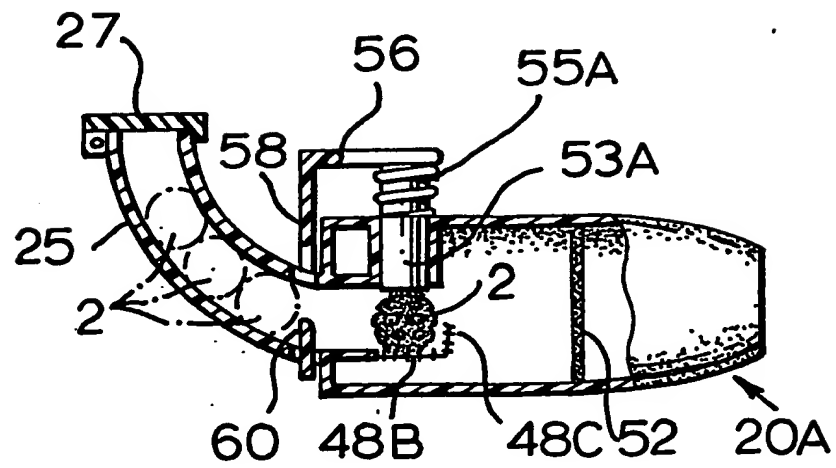


FIG.14



-1-

APPARATUS FOR USE IN INHALATION

This invention relates to a method and means for dispensing a medicament for use in inhalation.

It is known to provide an inhaler device for the administration of a drug used in the treatment of respiratory diseases, e.g. asthma, and it has been proposed to administer single dosage of drugs by providing "unit dose" capsules.

In our co-pending British Patent Application number 8914384.6 there is described a particular method of pre-piercing capsules of that type to readily facilitate access to the encapsulated medicament.

In accordance with the present invention there is provided a capsule for the containment of a medicament whereby the capsule is readily fracturable to allow egress of the medicament. There is further provided an inhalation device having means for fracturing a capsule contained therein.

In one aspect of the invention there is provided a medicament containing capsule comprising a shell formed with weakened portions whereby the shell is readily fracturable.

The shell may be made of a brittle material and the weakened portions may be in the form of areas of reduced cross section.

However, the capsule may not be formed with a shell, but may be aerated to provide microencapsulations which contain the medicament.

The capsules may be of any three-dimensional form, but are preferably spherical or substantially so. However, they may be of cuboid, hexagonal or generally cylindrical form, the form being such that will lend itself to automatic filling, capping and manipulating during the manufacturing operations.

In another aspect of the invention there is provided an inhalation device for use with fracturable capsules, wherein there is provided a body which includes means for locating a fracturable capsule, an air inlet port and an air outlet port and means adapted to impart a force to the capsule in order to fracture the shell.

The air outlet port may comprise a mouth piece.

The means for exerting pressure on the capsule may be a part of the body of the device which is hinged to provide a pincer-like action, or it may be a manually operable plunger device, or by means capable of a twisting action.

The inhalation device may be provided with means whereby only medicament entrained air passes into and through the outlet port and the means may include a filter

capable of preventing passage of parts of the fractured or fragmented shell.

The filter may be a mesh screen, and/or a spacer type device of the type described in our co-pending British Patent application number 8926543.3.

Various embodiments of the invention will now be described, by way of example only, with reference to the accompanying drawings in which:-

Figures 1 to 11 illustrate various "unit-dose" capsules according to one aspect of the invention,

Figure 12 is a perspective view of an inhaler according to a second aspect of the invention,

Figure 13 is a perspective view of an inhaler similar in some respect to that of Figure 12,

Figure 14 is a section view of an alternative embodiment of an inhaler.

In Figure 1 is shown a medicament containing capsule having a shell 2 comprising a body part 4 and a cap part 6. In manufacture, a single dose of prescribed medicament powder is inserted into the base part after which the cap is assembled thereon. The cap may be held frictionally on the base e.g. by shrinkage, or by an adhesive material, or by a band 8 as illustrated in

Figure 3. Alternatively the connection may be by means of the physical engagement of a projection on the cap with a groove in the base, or vice versa.

In some cases the base part 4, as seen in Figure 2 may, after being filled or part-filled with the medicament powder, be sealed by a cap or lid 10.

Other shapes of capsule are illustrated in Figures 4, 5 and 6 which show respectively substantially spherical, cuboid and hexagonal polyhedron forms, each having body portions 4 and caps 6.

In all the above cases the shell is made of a rigid but brittle material so that it can be readily crushed, fragmented or pulverized to release the medicament powder contained therein. The shell may be made of hard gelatine of the type used for oral drug preparations and specially formulated to have the required fracturing characteristics over a wide range of temperatures and humidities. With this in mind it may be treated before or after filling by dehydration or irradiation for example.

Alternatively the shell may be formed of moulded or compressed materials such as starch, lactose or other suitable pharmaceutically acceptable materials. These materials may include additives to facilitate capsule formation, during the manufacturing process of the capsules

and may also contain substances to impart the desired fragmentation characteristics, either directly or after additional treatment such as heat or irradiation.

Figures 7, 8, 9 and 10 illustrate various ways in which the shell is moulded or compressed into shapes that effect ready fragmentation, and at the same time facilitate high speed automatic manipulation during the processing and filling operations.

Figures 7 and 8 illustrate a spherical capsule which is formed with fracture lines 10 of reduced cross section, which assist in ready fragmentation of the shell when subjected to pressure.

The capsules illustrated in Figures 9 and 10 have their shells formed with indentations 12 which facilitate ready fragmentation to release the medicament.

The capsule 100 illustrated in Figure 11 has a number of microencapsulations or hollow spherical "bubbles" 102 and medicament is caused to be encapsulated within those "bubbles" during the manufacturing process.

Referring now to Figure 12, an inhaler 20 is illustrated and has a body 22 formed with an air inlet port 24, and an air outlet port 26. The outlet port is formed in a mouth piece 28.

The body is in two parts, a base part 30, and, connected by a hinge 32 thereto at the end distal from the mouth piece is an upper part 34.

The base part is formed with side walls 36 and an end wall 38. The upper part has side walls 40 and an end wall 42. When the hinged upper part 34 is closed on to the base part 30, the side walls 36, 40, the end walls 38, 42 and the mouth piece 28 together define a chamber 44.

Within the chamber 44 and mounted between the side walls of the inhaler is a capsule crushing mechanism 46 comprising a grid 48 supported by the base part 30 and a further grid 50 supported between the walls 40 of the upper part 34.

A filter, in the form of a wire or plastics mesh screen 52 is provided within the mouth piece 28. The plastic screen may be moulded in one with the body of the inhaler.

In use the upper part 34 is opened about its hinge 32 and the capsule 2 is placed on the grid 48. When the hinged upper part 34 is closed onto the base part 30, the grid 50 applies pressure on the capsule, with a "nutcracker" effect to cause the shell of the capsule to fragment or disintegrate and release the medicament powder into the chamber 44. Inhalation by

the patient through the mouthpiece 28 entrains the powder into the air stream and into the patient's airways.

The arrangement and design of the capsule shell is such that the fragmented parts of the shell are too large to pass through the filter 52.

In an alternative inhaler shown in Figure 13 the body 22A is in one piece and has an end wall 38A in which is formed an air inlet port 24A through which a capsule may be inserted to be seated on a grid 48A. A plunger 53 is provided above the grid 48A and is normally urged upwardly by a spring 55 to project through its locating hole 54 in the upper surface of the body 22A, being suitably retained therein. A screen 52 and mouth piece 28 are provided in the same way as in the inhaler described with reference to Figure 12.

In operation a capsule 2 is inserted through the port 24A to rest on the grid 48A. Digital pressure on the plunger 53 against the action of the spring is effective to fragment the capsule and release medicament into the inhaler from where it is entrained in the air stream by inhalation by the patient.

In both the embodiments of Figures 12 and 13 the grids 48 and 48A may be formed with a shallow depression to locate the capsules.

The screen 52 may be replaced by, or used in conjunction with, other types of filter devices, e.g. intermediate "spacer" type of filters between the body of the inhaler and the mouth piece, wherein the fragmented shell portions are centrifuged by the air stream to be temporarily retained by the filter device or devices.

A centrifugal separator may be located between the crushing grid 48A and the mesh screen 52 preferably below the crushing grid 48A. In this manner air entering through port 24A will drive the centrifuge.

Other arrangements of capsule fragmenting devices within the inhaler may be provided without departing from the invention, for example, by imparting a twisting action to part or parts of the inhaler, or to the capsule itself.

As a further example, a blade or blades may be provided in place of the grids 48, 50 of Figure 12, the closure of the hinged body portion causing splitting of the shell by the blades.

Similarly the plunger 53 of Figure 13 may have its lower part formed as, or provided with, a blade or wedge shaped section to have a splitting effect on the shell.

Although the examples illustrated in Figures 12

and 13 require individual placement of each capsule, there may be included in the inhaler device means whereby capsules may be readily or automatically fed into position for fracturing, e.g. from a magazine device.

Such an arrangement is illustrated in Figure 14 where an inhaler 20A is provided with a grid 48B and a plunger 53A. A magazine chute 25 with a lid 27 is loaded with capsules 2 and attached to the plunger 53A is an extension 56 having a downwardly depending tongue 58 and an upwardly depending tongue 60. The tongues 58 and 60 are arranged to pass through slots formed in the walls of the magazine chute 25. A spring 55A surrounds the plunger 53A and urges the plunger upwardly.

In use, the magazine chute 25 is loaded with capsules 2 and depression of the plunger 53A against the action of the spring 55A first causes the tongue 60 to be lowered out of its retaining engagement with the lowermost capsule within the chute. That capsule then enters the body of the inhaler and the uppermost tongue 58 moves into retaining position in the path of the next adjacent capsule. The plunger is then released to assume its position as seen in Figure 14, with the first capsule positioned axially below the plunger and retained by a lip 48C on the mesh 48B.

As the plunger is next depressed to crush the

capsule positioned between it and the mesh 48B, the next following capsule in the magazine chute is released as just described, and the sequence is repeated.

When the crushing device of Figure 13 is used with respect to capsules of the type seen in Figure 11, the material between the "bubbles" is crushed by the plunger 53 to release the encapsulated medicament so that it may be inhaled through the mouth piece 28.

The plunger may be provided with a control system which enables it to be depressed by a predetermined amount each time, the amount of depression determining the dosage of the medicament. The amount of depression may be determined, for example, by rotation of a screw threaded plunger, rotated according to requirements or by aratchet and pawl mechanism so arranged to give a pre-determined length of stroke to the plunger.

The illustrative embodiments of the invention have been described with reference to capsules containing powdered medicament; however, it is to be understood that the capsules may, of course, contain liquid or gaseous medicaments.

CLAIMS

1. A capsule for the containment of a medicament wherein the capsule is readily fracturable to allow egress of the medicament.
2. A capsule according to claim 1 wherein the capsule comprises a shell which is readily fracturable to allow egress of the medicament.
3. A capsule according to claim 2 wherein at least part of the shell is made of a brittle material.
4. A capsule according to claims 2 or 3 wherein the shell has weakened portions in the form of areas of reduced cross section.
5. A capsule according to claim 1 which is of three-dimensional form and constructed from at least two parts, and that will lend itself to automatic filling, capping and manipulating during manufacturing operations.
6. A capsule according to claim 1 wherein the medicament is encapsulated within the structure of the capsule.
7. An inhalation device for use with fracturable capsules wherein there is provided a body which includes means for locating a fracturable capsule, an air inlet port and an air outlet port and means adapted to impart a force to the capsule in order to fracture the capsule.

8. An inhalation device according to claim 7 wherein the air outlet port comprises a mouth piece.
9. An inhalation device according to claim 7 wherein the means for exerting pressure on the capsule is part of the body of the device which is hinged to provide a pincer-like action.
10. An inhalation device according to claim 7 wherein the means for exerting pressure on the capsule is a manually operable plunger device.
11. An inhalation device according to claim 7 wherein the means for exerting pressure on the capsule operates by means of a twisting action.
12. An inhalation device according to claims 7 to 11 inclusive wherein means are provided for ensuring that only medicament entrained air passes into and through the outlet port.
13. An inhalation device according to claim 12 wherein said means include a filter capable of preventing passage of parts of the fractured or fragmented shell.

14. An inhalation device according to claim 12 wherein the means include a cyclone separation device.

15. An inhalation device according to claim 12 wherein the filter is a mesh screen.

16. An inhalation device according to any of the above claims 7 to 15 wherein there is included means whereby capsules may be readily fed into position for fracturing.

17. An inhalation device according to claim 16 wherein the capsules are automatically fed into position from a magazine device.

18. An inhalation device according to any of the claims 7 to 17 wherein means are provided to fracture a capsule of the type according to claim 6 partially and sequentially.

19. A method of inhalation of a medicament whereby a medicament-containing capsule having a readily fracturable structure is placed within an inhalation device, manual manipulation of the device is effected to fracture the structure and the medicament is inhaled by suction through an air outlet port.

Patents Act 1977
Examiner's report to the Comptroller under
Section 17 (The Search Report)

Application number

9102252.5

Relevant Technical fields

(i) UK Cl (Edition K) A5T TBM TBE

(ii) Int Cl (Edition 5) A61M

Databases (see over)

(i) UK Patent Office

(ii)

Search Examiner

J A WALLIS

Date of Search

21 FEBRUARY 1992

Documents considered relevant following a search in respect of claims 7 AND 19 AT LEAST

Category (see over)	Identity of document and relevant passages	Relevant to claim(s)
X	GB 2151491 A (BOEHRINGER ETC) Breaking means 11 and lines 127-129, page 2	7,8,10-13 15 at least
X	GB 2142246 A (GLAXO ETC) Whole document pertinent	7-9,12,13 15,16,18 at least
X	GB 2129691 A (GLAXO ETC) Whole document pertinent	7-9,12,13 15,16,18 at least
X	GB 2064336 A (GLAXO ETC) Whole document pertinent	7,8,11,12 13,15,16, 18 at least
X	GB 1515265 (PIERRE FABIN) Whole document pertinent	7,8,11,12 16,19 at least
X	GB 1472650 (PAUL RITZAU ETC) Whole document pertinent nb lines 107-116, page 2	7,8-11,12 13,15,16, at least
X	GB 1331216 (I.S.F. ETC) Whole document pertinent	7,8,10, 12-15,16 at least

Category	Identity of document and relevant passages - 15 -	Relevant to claim(s)

Categories of documents

X: Document indicating lack of novelty or of inventive step.

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A: Document indicating technological background and/or state of the art.

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Patents Act 1977
Examiner's report to the Comptroller under
Section 17 (The Search Report)

Application number

9102252.5

Relevant Technical fields

(i) UK CI (Edition) Contd. from page 5

(ii) Int CI (Edition)

Databases (see over)

(i) UK Patent Office

(ii)

Search Examiner

J A WALLIS

Date of Search

21 FEBRUARY 1992

Documents considered relevant following a search in respect of claims

Category (see over)	Identity of document and relevant passages	Relevant to claim(s)
X	GB 588117 (HAYWARD-BUTT) Whole document pertinent	7,8,10,11 12,13,15, 19 at least
X	EP 0333334 A2 (HARRIS ETC) Whole document pertinent	7,8,9,12, 13,15,16, at least
X	US 4095596 (GRAYSON) Whole document pertinent	7,8,9,11 12,13,15, 19 at least

Category	Identity of document and relevant passages -17-	Relevant to claim(s)

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(i) UK CI (Edition K) B8C

(ii) Int CI (Edition 5) A61J; A61M

Databases (see over)

(i) UK Patent Office

(ii)

ONLINE DATABASES: WPI; CLAIMS

Search Examiner

MRS S CHALMERS

Date of Search

25.2.91

Documents considered relevant following a search in respect of claims

1-6

Category (see over)	Identity of document and relevant passages	Relevant to claim(s)
X	GB 2103564 (CANADIAN MINISTER) see capsule 10	1-3,6
X	GB 818365 (SCHERER) see page 2 lines 86-107 and figure 3	1-3,5
X	GB 676568 (DEHN) see capsules 12, 26, 52, 62, 72, 82, 102, 112, 132	1-3
X	GB 576047 (WELLCOME) whole document	1-3
X	GB 563011 (TRIGGS) see figure	1-3,5
X	GB 456471 (TENNANT) whole document	1-3
X	GB 428635 (BARBIANI) see eg page 1 lines 91-96	1-3
X	GB 354680 (GUILLISSEN)	1-4
X	EP 0040959 (AMERICAN STERILISER) see container 12	1-3

SF2(p)

Category	Identity of document and relevant passages	Relevant to claim(s)

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